

protein containing an N-terminal extension of acidic amino acid residues, thereby forming an acidic N-terminal extension of a protein-protein interaction surface or of a dimerization or multimerization surface of said acidically modified nucleic acid binding protein, said acidic N-terminal extension allowing said acidically modified nucleic acid binding protein to dimerize or multimerize with a normal cellular protein, under conditions allowing for the expression of said acidically modified nucleic acid binding protein in cells of the plant or non-human animal; and

(b) expressing the acidically modified nucleic acid binding protein in the cells of the plant or non-human animal, thereby allowing multimeric or dimeric complexation between said expressed acidically modified nucleic acid binding protein and a cognate naturally occurring cellular protein.

Please add the following new claims 29-56:

29. (New) The method according to claim 28, wherein the isolated DNA molecule is introduced into the cells in a vector.

30. (New) The method according to claim 29, wherein the vector is a prokaryotic, eukaryotic or viral vector.

31. (New) The method according to claim 29, wherein the vector comprises a cell- or tissue-specific promoter, being inducible or noninducible, a transcription initiation site, a transcription termination site, an origin of replication, and a polyadenylation site, for expression in host cells.

32. (New) The method according to claim 30, wherein the vector

is selected from the group consisting of Simian Virus 40 (SV40) vector, adenovirus vector, vaccinia virus vector and adeno-associated virus vector.

33. (New) The method according to claim 28, wherein the encoded acidically modified nucleic acid binding protein is an acidically modified bZIP protein.

34. (New) The method according to claim 33, wherein the encoded acidically modified bZIP protein is selected from the group consisting of Fos, Jun, GCN4 (general control of nitrogen and purine metabolism factor-4), VBP (vitellogenin gene binding protein), GBF-1 (G-box factor-1), opaque, DBP (D-box binding protein), CHOP-10 (C/EBP homologous protein-10), CREB (CRE binding protein), C/EBP (CCAAT/enhancer binding protein), PAR (proline- and acidic amino acid-rich protein), and ATF2 (activating transcription factor-2).

35. (New) The method according to claim 28, wherein the encoded acidically modified nucleic acid binding protein is an acidically modified basic helix-loop-helix (bHLH) protein.

36. (New) The method according to claim 35, wherein the encoded acidically modified bHLH protein is selected from the group consisting of c-myc, n-myc, i-myc, max, mad, ID, MyoD1 (myogenic differentiation factor-1), E12 (immunoglobulin enhancer binding protein-12), AP-4 (activating enhancer binding protein-4), TFE3 (transcription factor E3), USF (upstream stimulatory factor), and FIP (Fos interacting protein).

37. (New) The method according to claim 28, wherein the encoded acidically modified nucleic acid binding protein has an amino acid sequence as shown in any one of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:29, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:57, or SEQ ID NO:64.

38. (New) A transgenic non-human mammal all of whose germ cells and somatic cells contain a recombinant acidic dominant negative polynucleotide sequence introduced into said mammal, or an ancestor of said mammal, at an embryonic stage, wherein the expression product of said acidic dominant negative sequence stably dimerizes or multimerizes with a normal cellular protein.

39. (New) The mammal according to claim 38, wherein transcription of said acidic dominant negative polynucleotide sequence is controlled by a tissue-specific promoter sequence.

40. (New) The mammal according to claim 38, wherein the acidic dominant negative polynucleotide sequence encodes an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:29, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42,

SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:57 and SEQ ID NO:64.

41. (New) The mammal according to claim 38, wherein the acidic dominant negative polynucleotide sequence is selected from the group consisting of SEQ ID NO:6, SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28 and SEQ ID NO:32.

42. (New) The mammal according to claim 38, wherein the acidic dominant negative polynucleotide sequence encodes a 3heptadF- (SEQ ID NO:37) C/EBP sequence (SEQ ID NO:58).

43. (New) The mammal according to claim 39, wherein the promoter sequence is an adipose fatty acid binding protein promoter sequence.

44. (New) The mammal according to claim 43, wherein the adipose fatty acid binding protein promoter sequence is aP2.

45. (New) The mammal according to claim 43, wherein the adipose fatty acid binding protein promoter sequence controls gene expression in adipose tissue.

46. (New) The mammal according to claim 39, wherein the promoter sequence is a whey activating protein promoter sequence.

47. (New) The mammal according to claim 46, wherein the whey activating promoter sequence controls gene expression in mammary or breast

tissue.

48. (New) The mammal according to claim 38, said mammal being selected from the group consisting of rodents, sheep, pigs and primates.

49. (New) The mammal according to claim 38, said mammal being a rodent.

50. (New) The mammal according to claim 49, said rodent being a mouse or a rat.

51. (New) A transgenic non-human mammal whose germ cells and adipose tissue cells contain an expression system comprising:

(a) a first DNA sequence coding on expression for an acidic dominant negative b-Zip or bHLH protein; said acidic dominant negative protein having a biological activity of a dominant negative to a cellular protein; and

(b) a promoter functional in said adipose tissue cells, whereby said mammal, under conditions conducive to expression, expresses said acidic dominant negative protein in adipose tissue of said mammal.

52. (New) The transgenic non-human mammal according to claim 51, wherein the acidic dominant negative b-Zip or bHLH protein comprises an N-terminal acidic amino acid sequence extension selected from the group consisting of SEQ ID NOS:35-42.

53. (New) The transgenic non-human mammal according to claim

51, wherein is acidic dominant negative b-Zip protein is 3heptadF-C/EBP.

54. (New) A method of producing a transgenic non-human mammal capable of expressing a protein which has a biological activity of an acidic dominant negative to a cellular protein, said method comprising chromosomally incorporating a polynucleotide sequence encoding the protein into the genome of a non-human mammal so that said genome comprises an expression system comprising:

(a) a first DNA sequence coding on expression for an acidic dominant negative b-Zip or bHLH protein; said acidic dominant negative protein having a biological activity of a dominant negative to a cellular protein; and

(b) a promoter functional in adipose tissue cells, whereby said mammal, under conditions conducive to expression, expresses said acidic dominant negative protein in adipose tissue of said mammal.

55. (New) The method according to claim 54, wherein the acidic dominant negative b-Zip or bHLH protein comprises an N-terminal acidic amino acid sequence extension selected from the group consisting of SEQ ID NOS:35-42.

56. (New) A transgenic non-human mammal which is a founder mammal prepared by the method of claim 54, or progeny of said founder mammal, wherein said transgenic mammal, under conditions conducive to expression, expresses said protein in adipose tissue of said mammal so as to affect the normal production of fat tissue.